wherein said DNA sequence is operably linked to said promoter

and wherein said DNA molecule forms transcripts through which an endogenous citrate synthase activity can be suppressed; and

(b) regenerating the transgenic plant from said transgenic cell, wherein the reduced citrate synthase activity of said transgenic plant inhibits flower formation compared to flower formation in a wild type plant.

REMARKS

The Amendments

Applicants have amended claims 84 and 112. Applicants have amended claim 84 to recite a DNA molecule comprising all or part of a DNA sequence of a coding region for a citrate synthase and that the DNA sequence is at least 15 basepairs in length. Support for these amendments may be found throughout the specification. See e.g., page 8, lines 10-13.

Applicants have amended claim 112 to recite that the reduced citrate synthase activity of the transgenic plant inhibits flower formation compared to flower formation in a wild type plant. Support for these amendments may be found throughout the specification, e.g., at page 5, line 24 to page 6, line 12; Example 3 (page 37, line 6 to page 41, line 34); and Example 8 (page 44, line 7 to page 45, line 34).

The Drawings

The drawings have been objected to by the Draftperson for reasons provided in the Notice of Draftperson's Patent Drawing Review. Applicants stand ready to provide corrected final drawings upon allowance of the present application.

The Restriction Requirement

The Examiner states that the applicant's traversal of the restriction requirement between Groups I, III and IV is not persuasive because the basis for restriction is lack of unity of invention. The Examiner further states that because this application was filed under 37 C.F.R. § 371, there is no standard of burden required for maintaining a restriction where the Office holds that two or more inventions lack unity of invention therebetween. The Examiner has made the restriction final.

Applicants affirm their election of Group I, Species IV, which were elected in the Applicant's Response filed October 7, 1999. Applicants reserve the right to petition the Commissioner to review the restriction requirement under 37 C.F.R. § 1.144.

The Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 84-85, 88, 94-99, 112 and 115-117 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner contends that it is not clear whether the parenthetical enclosing "EC No. 4.1.3.7" is intended to limit the citrate synthase in claim 84. One having ordinary skill in the art would understand that an EC number refers to the Enzyme Classification number, which is an internationally accepted nomenclature that identifies the catalytic property of an enzyme and has been in place since 1961. See Exhibit B. Specifically, the skilled artisan would know that "EC No. 4.1.3.7" refers to an enzyme that catalyzes the following reaction: citrate + CoA = acetyl-CoA + H_2O +

oxaloacetate, which enzyme is commonly called citrate synthase (see Exhibit C). Accordingly, the recitation of "EC No. 4.1.3.7" in claim 84 is clear.

The Examiner also asserts that claim 84 is indefinite because the coding region for a citrate synthase is recited on lines 2-3; however, on line 6, the claimed DNA molecule is recited to be as small as 15 basepairs, and the coding region for each of the known of disclosed citrate synthase genes are all greater than 15 basepairs. Applicants have obviated this rejection by amending claim 84 to recite a DNA molecule comprising all or part of a DNA sequence of a coding region for a citrate synthase, wherein the DNA sequence is at least 15 basepairs in length.

Claims 85, 88, 91 and 94-99 depend either directly or indirectly from claim 84 and thus incorporate the amendments to claim 84. Accordingly, applicants request that the rejection of claims 84, 85, 88, 91 and 94-99 under 35 U.S.C. § 112, second paragraph, be withdrawn for the reasons provided above.

The Examiner contends that claim 112 does not provide a concluding step by which the inhibition of flower formation in a transgenic plant compared to flower formation in a wild type plant is achieved. Applicants have obviated this rejection by amending claim 112 to recite that the reduced citrate synthase activity of the transgenic plant inhibits flower formation compared to flower formation in a wild type plant.

Claims 115-117 depend either directly or indirectly from claim 112 and thus incorporate the amendments to claim 112. Applicants request that the rejection of claims 112 and 115-117 under 35 U.S.C. § 112, second paragraph, be withdrawn for the reasons provided above.

The Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claims 71, 74-76, 79-85, 88, 91, 94-101, 104-105, 108, 111-112 and 115-120 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Unger et al., Plant Molecular Biology 13:411-418, 1989 (hereafter "Unger") in view of Shewmaker et al., U.S. Patent No. 5,107,065 (hereafter "Shewmaker").

The Examiner states that Unger teaches a citrate synthase protein and gene therefor from *Arabidopsis thaliana*. The Examiner states that the citrate synthase protein taught by Unger exhibits over 65% "structural match" to SEQ ID NO: 2 and the DNA sequence exhibits nearly 30% overall structural identity to SEQ ID NO: 1, including stretches of at least 15 basepairs that exhibit 100% identity. The Examiner admits that Unger does not teach fusing the citrate synthase gene or portion thereof in antisense relation to a plant functional promoter.

The Examiner contends that Shewmaker states that regulation of expression in plant cells may be achieved by integrating a DNA sequence in antisense orientation to reduce the functioning of naturally-existing DNA. The Examiner further contends that Shewmaker states that the reduction is useful for modulating the phenotypic properties of a plant, including modulation of metabolic pathways. The Examiner states that Shewmaker teaches that a DNA sequence of at least 15 basepairs may be used and the DNA sequence may be fused to a plant-functional promoter. The Examiner contends that inhibition of flowering may be the phenotypic property desired.

The Examiner contends that it would have been obvious to one of ordinary skill in the art to have used the DNA sequence for the citrate synthase gene taught by Unger following the teaching of Shewmaker to produce a DNA construct

comprising a portion of at least 15 basepairs from or with at least 65% identity to a DNA sequence encoding the citrate synthase fused to a plant functional promoter. The Examiner states that one would have been motivated to do this because Unger teaches the importance of citrate synthase for studying the balance of energy-generating processes available to photosynthetic cells. The Examiner further states that one would have expected that the use of antisense RNA would inhibit citrate synthase with a reasonable expectation of success. The Examiner admits that Unger does not teach the relationship between citrate synthase and flower formation, but states that one skilled in the art would have found it obvious to use antisense RNA for citrate synthase for reasons such as studying the balance of energy-generating processes available to photosynthetic cells or for modulating metabolic pathways. Applicants traverse.

Obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988) (citing *ACS Hosp. Sys.*, 732 F.2d at 1577, 221 USPQ at 933). The teaching or suggestion to combine must come from the prior art and not from the applicant's own disclosure. In addition, "the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453, 1458 (Fed. Circ. 1998). In the present case, there is no such teaching or suggestion supporting the combination of Unger and Shewmaker, as asserted by the Examiner.

Neither Unger nor Shewmaker, either alone or together, suggest reducing citrate synthase activity by antisense DNA or, in fact, by any other mechanism. Unger states only that the authors are interested in characterizing

expression-controlling sequences of genes involved in energy-generating processes and in gathering information on targeting of polypeptides into plant mitochondria. See Unger, p. 411, right column. Neither of these problems could reasonably be addressed using an antisense DNA molecule of the invention. Thus, there is no explicit or implicit motivation in Unger to look to the teachings of Shewmaker.

Similarly, Shewmaker states only that one may use antisense DNA "so that the production of individual proteins may be reduced, multi-enzyme processes modulated, particular metabolic pathways modulated or inhibited in preference to one or more other metabolic paths, production of non-proteinaceous products reduced, cell differentiation modified, and the like." Shewmaker, col. 2, lines 27-32. There are thousands of proteins and non-proteinaceous products expressed in cells, and hundreds or thousands of cellular multi-enzyme processes and metabolic pathways. Nothing in Shewmaker teaches or suggests using antisense to reduce the activity of any enzyme of the citric acid cycle, much less to reduce the activity of a particular enzyme, citrate synthase. Thus, there is no motivation in Shewmaker to look to the teachings of Unger.

Accordingly, there is no motivation in Unger or Shewmaker, either alone or taken together, to produce a DNA molecule comprising a portion of at least 15 basepairs from or with at least 65% identity to a DNA sequence encoding the citrate synthase fused to a plant functional promoter; to produce vectors, host cells, transgenic plant cells and transgenic plants comprising the DNA molecule; or to develop methods of reducing citrate synthase in a transgenic plant using the DNA molecule. In addition, there was no knowledge generally available to one of ordinary skill in the art at the time the invention was made to modify or combine Unger with Shewmaker to arrive at the claimed invention.

In light of the foregoing, applicants request that the rejection under 35 U.S.C. § 103(a) of claims 71, 74-76, 79-85, 88, 91, 94-101, 104-105, 108, 111-112, 115-120 over Unger in view of Shewmaker be withdrawn.

The Examiner also cites Bourque et al., U.S. Patent No. 5,354,854 (hereafter "Bourque") for an alternative teaching of antisense technology applied to regulate expression of endogenous genes in plants including metabolic enzymes. Bourque fails for the same reasons as Shewmaker.

Objections

The Examiner has objected to claim 77 for being dependent on rejected claim 71, but states that this claim would be allowable if rewritten in independent form.

As discussed above, the rejection of claim 71 under 35 U.S.C. § 103(a) may properly be withdrawn. Thus, claim 77 is no longer dependent on a rejected claim.

CONCLUSION

In light of the foregoing amendments and remarks, applicants request that the Examiner withdraw all outstanding rejections and grant allowance of the pending claims.

The Examiner is invited to telephone applicants' representatives regarding any matter that may be handled by telephone to expedite allowance of the pending claims.

Respectfully submitted,

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I hereby certify that this [illegible] on July 17, 2001

EXHIBIT A

84. (Amended) A DNA molecule comprising

(i) all or part of a DNA sequence of a coding region for a citrate synthase (EC No. 4.1.3.7.) of a plant of the *Solanaceae* family or the *Chenopodiaceae* family operably linked to

(ii) suitable elements controlling the transcription of said coding region in procaryotic and/or eucaryotic cells;

wherein said DNA [molecule] sequence is at least 15 basepairs in length and, when integrated into the genome of a cell of a plant, is transcribed to yield RNA that reduces the activity of an endogenous citrate synthase in said cell of a plant in comparison to the citrate synthase activity of a wild type plant cell.

112. (Amended) A process for inhibiting flower formation in a transgenic plant compared to flower formation in a wild type plant, wherein the citrate synthase activity in the cells of said transgenic plant are reduced compared to the citrate synthase activity in wild type plant cells, comprising the steps of

(a) introducing into a plant cell a recombinant double-stranded DNA molecule to generate a transgenic plant cell, said DNA molecule comprising

(i) a promoter functional in plant cells; and

(ii) a DNA sequence coding for citrate synthase or a part of said DNA sequence, which is at least 15 bp and is sufficient in length to suppress endogenous citrate synthase activity,

wherein said DNA sequence is operably linked to said promoter

and wherein said DNA molecule forms transcripts through which an endogenous citrate synthase activity can be suppressed; and

(b) regenerating the transgenic plant from said transgenic cell, wherein the reduced citrate synthase activity of said transgenic plant inhibits flower formation compared to flower formation in a wild type plant.